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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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EXAMINER	
MURPHY, J	
ART UNIT	PAPER NUMBER
1746	5

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Offic Action Summary	Application No. 09/607,156	Applicant(s) LOETSCHER ET AL.	
	Examiner Joseph F Murphy	Art Unit 1646	

-- Th MAILING DATE of this communication appears on the cover sheet with the correspondenc address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

1)☒ Responsive to communication(s) filed on *14 September 2000* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *16,17,19-21 and 60-84* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *16-17, 19-21, and 60-84* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a)☐ All b)☐ Some * c)☐ None of the CERTIFIED copies of the priority documents have been:

1.☐ received.

2.☐ received in Application No. (Series Code / Serial Number) _____ .

3.☐ received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. & 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
18) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other: *Sequence Comparison A, B* .

DETAILED ACTION

Claims 1-15, 18 and 22-59 were cancelled, claims 16-17, 19-21 were amended, and new claims 21-84 were added in paper No. 2, 6/29/2000.

Claims 16-17, 19-21 and 60-84 are under consideration.

Specification

The abstract of the disclosure is objected to because it is too long. Correction is required. See MPEP § 608.01(b).

Claim Rejections - 35 USC § 112 first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 16-17, 19-21 and 60-84 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a substantially purified polypeptide comprising an amino acid sequence set forth in SEQ ID NO: 2, does not reasonably provide enablement for amino acid sequences that are variants of said sequences. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims 16-17, 61-65, 67-68 are overly broad in the recitation of "variants". There is not adequate guidance as to the nature of the variants which Applicants claim. Since variants of polypeptides can include single amino acids, the claim can be reasonably interpreted to include any substantially purified polypeptide that is smaller in size than the polypeptide of SEQ ID NO: 2. There is no guidance provided in the specification as

to the relationship between the structure of CXCR3 and its function. Without this information, it would require undue experimentation for one of skill in the art to generate a substantially purified CXCR3 polypeptide, other than that which is exemplified in the specification. See In re Wands, 858 F.2d at 737, 8 USPQ2d at 1404. The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. The factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue" include, but are not limited to: (1) the breadth of the claims; (2) the nature of the invention; (3) the state of the prior art; (4) the level of one of ordinary skill; (5) the level of predictability in the art; (6) the amount of direction provided by the inventor; (7) the existence of working examples; and (8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. Given the breadth of claims 16-17, 61-65, 67-68 16-17, 61-65, 67-68 in light of the predictability of the art as determined by the number of working examples, the level of skill of the artisan, and the guidance provided in the instant specification and the prior art of record, it would require undue experimentation for one of ordinary skill in the art to make and use the claimed invention. Claims 19-21, 66, 69-84 are rejected insofar as they depend on the recitation in claims 16-17, 61-65, 67-68 of "variant" of a CXCR3 polypeptide.

Claims 63-64, 83-84 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a substantially purified polypeptide

comprising an amino acid sequence set forth in SEQ ID NO: 2, does not reasonably provide enablement for a variant having at least 90% amino acid sequence identity to SEQ ID NO: 2. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims 63-64 and 83-84 are overly broad in the recitation of "at least about 90% identical" since no guidance is provided as to which of the myriad of polypeptide species encompassed by the claim will retain the characteristics of a CXCR3. In the specification (page 14, lines 23-23), Applicants disclose that variants of the polypeptide include those having deletions relative to the mature mammalian CXCR3, without disclosing any actual or prophetic examples on expected performance parameters of any of the possible muteins of CXCR3. However, it is known in the art that even single amino acid changes or differences in the amino acid sequence of a protein can have dramatic effects on the protein's function. For example, Mikayama et al. (1993) teaches that the human glycosylation-inhibiting factor (GIF) protein differs from human migration inhibitory factor (MIF) by a single amino acid residue (page 10056, Figure 1). Yet, despite the fact that these proteins are 90% identical at the amino acid level, GIF is unable to carry out the function of MIF, and MIF does not exhibit GIF bioactivity (page 10059, second column, third paragraph). It is also known in the art that a single amino acid change in a protein's sequence can drastically affect the structure of the protein and the architecture of an entire cell. Voet et al. (1990) teaches that a single Glu to Val substitution in the beta subunit of hemoglobin causes the hemoglobin molecules to associate with one another in such a manner that, in homozygous individuals, erythrocytes are altered from their

normal discoid shape and assume the sickle shape characteristic of sickle-cell anemia, causing hemolytic anemia and blood flow blockages (pages 126-128, section 6-3A and page 230, column 2, first paragraph).

There is no guidance provided in the specification as to how one of ordinary skill in the art would generate a nucleic acid sequence encoding a CXCR3 polypeptide other than those exemplified in the specification. See In re Wands, 858 F.2d at 737, 8 USPQ2d at 1404. The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. The factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue" include, but are not limited to: (1) the breadth of the claims; (2) the nature of the invention; (3) the state of the prior art; (4) the level of one of ordinary skill; (5) the level of predictability in the art; (6) the amount of direction provided by the inventor; (7) the existence of working examples; and (8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. Given the breadth of claims 63-64 and 83-84 in light of the predictability of the art as determined by the number of working examples, the level of skill of the artisan, and the guidance provided in the instant specification and the prior art of record, it would require undue experimentation for one of ordinary skill in the art to make and use the claimed invention.

Claim 16 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled

in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claim 16 is not enabled for a protein, encoded by a nucleic acid, wherein the nucleic acid hybridizes to second nucleic acid, and also hybridizes to the complement of the second nucleic acid. The complement of the second nucleic acid would have the identical sequence to the first nucleic acid. It would not be possible for the first nucleic acid to hybridize to itself.

Claim Rejections - 35 USC § 112 second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 16-17, 19-21 and 60-84 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 16 recites the term "high stringency", which is a conditional term and renders the claim indefinite. The metes and bounds of the claim thus cannot be ascertained. This rejection could be obviated by supplying specific conditions supported by the specification which Applicant considers to be "high stringency".

The term "selectively" in claims 16-17, 61-64 is a relative term which renders the claim indefinite. The term "selectively" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. Claims 65-84 are rejected insofar as they depend on the recitation of the term "selectively".

Claim 16 is vague and indefinite because it is unclear how a nucleic acid could hybridize to both a second nucleic acid, as well as to a sequence complementary to the second nucleic acid. The sequence complementary to the second nucleic acid would presumably have a sequence nearly identical to the first nucleic acid itself. Absent some palindromic sequences, it is unclear how the first nucleic acid would bind to itself.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 16-17, 19-21 and 60-84 are rejected under 35 U.S.C. 102(a) as being anticipated by Marchese et al. (1995).

Marchese et al. teaches the amino acid sequence of 3 G protein-coupled receptors (page 337 and 338, Figure 1). The nucleic acid sequence encoding GPR9 is 71.1% homologous to the polynucleotide sequence set forth in SEQ ID NO: 1 (see Sequence Comparison A, attached). Since GPR9 is disclosed as able to bind chemokines (page 335, column 2, second paragraph), and can be considered a "functional variant", based on the indefinite nature of that term (see above) the polynucleotide sequence disclosed in Marchese et al. meets the limitations of claims 16-17. The amino acid sequence disclosed in Marchese et al. has 100% amino acid identity to the amino acid sequence set forth in SEQ ID NO: 2 of the instant application (see Sequence Comparison B, attached),

thereby anticipating claims 20 and 63. Claims 19 and 21 are drawn to a protein encoded by SEQ ID NO: 1, which is 100% identical (at the amino acid level) to the protein disclosed in Marchese et al., therefore, claims 19 and 21 are anticipated. Since the structures of the proteins are identical, it would be an inherent property of the protein disclosed in Marchese et al. to bind IP-10 and Mig. The specification (page 16, line 31) states that a fusion protein comprises CXCR3 as a first moiety, and the second moiety may be, inter alia, an amino acid. Due to the recitation in the claim of "variant", the amino acid sequence disclosed in Marchese et al. as GPR 14 fits the limitations of a functional variant which is at least one amino acid longer than SEQ ID NO: 2 of the instant application (see page 339, column 1, first paragraph, which discloses that GPR14 is 386 amino acids, as compared to SEQ ID NO: 2, which is 368 amino acids long). Thus claims 60-62 and 64 are anticipated. Since that portion of the polypeptide which can be considered a fusion of the variant of the polypeptide set forth in SEQ ID NO: 2 is 18 amino acids longer, this could serve as an epitope tag, thus anticipating claims 65-84.

Conclusion

No claim is allowed.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph F. Murphy whose telephone number is 703-305-7245. The examiner can normally be reached on M-F 7:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached on 703-308-6564. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-308-0294 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Joseph F. Murphy, Ph. D.
Patent Examiner
Art Unit 1646
December 13, 2000

Prema Mertz
PREMA MERTZ
PRIMARY EXAMINER